

- (21) Application No. 24371/76 (22) Filed 11 Jun. 1976 (19)
 (23) Complete Specification Filed 25 May 1977
 (44) Complete Specification Published 11 Oct. 1978
 (51) INT. CL.² G01N 21/00
 (52) Index at Acceptance
 G1A 203 20Y 269 341 369 402 403 407 469 471 521 52Y
 530 53Y 548 549 552 55Y 580 581 589 58Y 627 790
 798 799 79Y CD E89 E9X R6 R7 R8
 (72) Inventors: Ian Kenneth Pasco
 David Neil Waters



(54) DETERMINING MONOMER CONTENT IN PMMA ELEMENTS

(71) We, COMBINED OPTICAL INDUSTRIES LIMITED, a British Company, of 200 Bath Road, Slough, Berkshire SL1 4DW, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

- 5 This invention is concerned with the manufacture of optical elements moulded of polymethylmethacrylate (hereinafter "pmma"), and is particularly concerned with a method of, and apparatus for, determining the content of free monomer in such elements. 5

It is known to mould optical elements in pmma. These elements almost always contain some free monomer (i.e. methyl methacrylate) trapped within the polymer lattice. For most purposes, the presence of this monomer can be ignored since although it is known that over the course of time, or in the presence of certain liquids, the monomer migrates to the surface of the element and so could contact the user, the amounts involved and the likelihood of harm being so caused, are very small. 10

However, for one particular use, the presence of monomer in pmma optical elements has to be very carefully controlled, and that is in the case of optical elements which are to be implanted in human tissue. It has been found that, in such cases, the monomer content has to be kept very low. Whilst there is as yet no officially recognised maximum level, it is thought that levels of about 3.0% by weight may be unacceptable in that damage has been caused to human tissue. For safety purposes, it seems likely that the maximum safe monomer content will be below 1%, and preferably below about 0.5%, by weight. 15 20

Pmma lens implants for human eyes are very small, and commonly weigh about 10 mg. In the interests of safety, it is necessary to test each lens implant individually to ensure that its monomer content is acceptably low rather than merely test one or two samples from a batch. So far as we are aware as a result of extensive investigations and enquiries, there is no currently available technique capable of reliably analysing these very small lenses (without any destruction or impairment of the lenses) for the even smaller monomer contents therein. Most non-destructive analytical techniques either require a much larger sample or else cannot reliably detect the monomer in the presence of the polymer, at such low concentrations (a concentration of 0.3% being equivalent to 0.03 mg of monomer in a 10 mg lens). 25

We have now devised a method of (and apparatus for) assaying articles of pmma, particularly but not exclusively implant lenses of pmma, for their monomer content, which method and apparatus are reliably sensitive to monomer contents well below the likely critical levels, and which can be used to analyse non-destructively individual implant lenses weighing of the order of 10 mg each. 30

According to the invention, there is provided a method of non-destructively assaying an article of polymethylmethacrylate for the free monomer content thereof, which comprises irradiating the article with substantially monochromatic light of a wavelength such as to give rise to, in the Raman spectrum, a pair of lines, one line arising from the monomer alone and the other from both the monomer and the polymer; determining the said pair of lines in the Raman spectrum of the irradiated article and thereby assaying the monomer content in the article 35 40

The invention also includes apparatus for non-destructively assaying an article of polymethylmethacrylate for the free monomer content thereof, which comprises a laser, means for mounting the article in the light path from the laser, a Raman spectrograph for observing the Raman spectrogram of the irradiated article; and means for automatically comparing the intensities of two pre-selected lines in the spectrogram and determining therefrom the monomer content of the 45

article.

We prefer to use a tuned laser, for example an argon-krypton laser tuned to one of the following spectral lines 647.1, 514.5 or 488.0 nano-metres, one suitable laser being of the type CRM52GMG. Other lasers and/or spectral lines can be used. When a pmma implant lens is exposed to such radiation, a Raman spectral line appears at $1730 \pm 10 \text{ cm}^{-1}$, which is due entirely to the presence of a carbonyl group. Both the polymer and the free monomer contain carbonyl groups. The lens also shows a Raman line at $1640 \pm 10 \text{ cm}^{-1}$, and this is due to the presence therein of a carbon-carbon double bond. Such a bond is present only in the monomer and not in the polymer. By measuring the intensities of these lines and from standard results (obtained, for example, by destructive analysis of larger samples of pmma) the amount of monomer can be determined.

Whilst we refer above to the pair of lines which we have found to be particularly suitable for use, it is possible that there may be other pairs of Raman spectral lines which could be used in the same manner as those described above, and the invention therefore includes, in its broader aspects, the use of such lines. Furthermore, whilst the invention has been conceived and proposed in respect of a particular problem associated with small implant lenses, it is nevertheless equally applicable to larger mouldings of pmma which could, possibly, be analysed by conventional known techniques. These larger mouldings need not necessarily be for optical purposes.

In the method of the invention, it is convenient to provide for automatic reading of the intensities of the two lines concerned and automatic calculation of the desired result (e.g. monomer content or, more simply, whether or not monomer content is below a permitted maximum). This automation can be achieved using known technology which, in itself, forms no part of the present invention.

In order that the invention may be more fully understood, one embodiment thereof will now be described, by way of illustration only, with reference to the accompanying drawings, in which:—

Figure 1 is a diagrammatic schematic illustration of one arrangement of apparatus for carrying out the method;

Figure 2 is a schematic illustration of one suitable arrangement, in more detail;

Figure 3 is a block diagram of one suitable control arrangement;

Figure 4 shows by way of example only, the relevant parts of two Raman spectra; and

Figure 5 is a graph of monomer content against ratio of Raman peak heights.

Referring to Figure 1, there is shown a laser 1, the lens implant sample 2, and a spectrograph 3. Laser 1 emits monochromatic beam 4 and spectrograph 3 receives the Raman emission (and reflected light) 5. As illustrated, the spectrograph 3 is at right angles to the laser beam 4, but (as is well known in Raman techniques) it need not be. It can, for example, be directly in line with (coaxial with) beam 4.

Figure 2 shows a generally similar arrangement but in greater detail. Laser 1 provides a monochromatic beam 4 which is reflected by mirror 10 and passes through filter 11 before impinging on lens implant sample 2. The Raman emission 5 enters double monochromator spectrograph 3, where it passes through slit 12 and is reflected by mirror 13 auto diffraction grating 14, from whence it passes to mirror 15 and thence to diffraction grating 16 whereafter it enters detector 17 in the detection and display unit 18. The results may be shown in chart form on chart display 19.

The use of the apparatus of Figures 1 and 2 will be clear to those skilled in the art and no further description thereof will therefore be given.

The block diagram of Figure 3 is essentially self-explanatory. Scanning of the spectrum, and in particular the two lines of interest, is automatically controlled and the readings so obtained converted into a direct read-out in the desired form. For example, the read-out may simply be "YES/NO" as to the acceptability of any lens (according to whether its monomer content is below the maximum permissible level chosen) or it may be the actual monomer level in the lens sample. The apparatus can include means for moving the lens sample, after analysis, to one or two stations depending on whether it is acceptable or not.

For example, two individually actuable push rods may be provided to push the lens either one way or the other depending on whether it is an acceptable lens or not.

Figure 4 shows the relevant parts of two spectra. Part A shows the spectrum obtained on a sample A of pmma of unknown monomer content, Part B shows the spectrum obtained on a sample whose monomer content had previously been calculated (by chemical analyses of at least two different types) to be $(1.0 \pm 0.1)\%$ by weight. By comparing the two spectra, the monomer content in the sample A can be calculated to be $(1.9 \pm 0.1)\%$. The sample was then analysed chemically and found to contain this quantity of monomer, to a good approximation.

In carrying out the method of the invention, it may be convenient to use a "standard curve" setting out the relationship between the ratio of Raman peak heights of the two lines in question and the amount of monomer in the sample under test. By observing the Raman peaks, it is then possible to read off from the standard curve the monomer content of the sample. Such a curve is shown in Figure 5 of the accompanying drawings, and its manner of preparation will now be described, by way of illustration only.

Discs were made of commercially available high purity pmma (I.C.I. "CQ" acrylic). The discs were divided into five groups A to E, and treated as follows. Groups A and B were immersed in boiling water for 9 hours. This treatment extracts monomer from the discs. The Raman spectrograms of these discs were then obtained (by at least three readings on each group) and the ratios of the peak heights of the two lines in question (see below) were measured.

The Raman spectrograms of the Group C discs were obtained and the ratios of the peak heights determined.

The Groups D and E discs were exposed to monomer vapour for 72 hours and were then examined and their Raman peak height ratios determined.

Each Group of discs was then subjected to assay by a gas chromatographic technique as follows. Standard solutions were made up of monomer in solvent (butyl acetate), of varying concentrations, and these solutions subjected to gas chromatography. A graph was plotted (which was substantially linear) between the ratio of monomer to solvent and the ratio of the peak heights of monomer to solvent and the gas chromatograph.

Then, for each of Groups A to E, known weights of the discs were dissolved in acetone and a known amount of a solution of the gas chromatograph solvent (used above) was added. The pmma reprecipitated. After shaking gently for 1 hour, a gas chromatogram of the clear supernatant was obtained. From the ratio therein of the peak height of monomer to solvent, the amount of monomer could be calculated using the graph previously prepared.

From these results, which are summarised below, the "standard curve" of Figure 5 was obtained. In Figure 5, the continuous line is a slight curve, and the discontinuous line is straight.

Results

Group	Raman Ratio	Gas Chromatography W/W% monomer in sample
A	0.042	0.280
B	0.042	0.269
C	0.084	0.875
D	0.269	3.80
E	0.434	5.55

The Raman spectra were recorded with a Spex 'Ramalab' Raman spectrometer, with excitation by a Coherent Radiation Laboratories model 52 MG argon-krypton laser. The line at 541.5nm was generally used for excitation, with an incident power at the sample of the order of 60mw. A plano-concave cylindrical lens was used in conjunction with the normal spherical condensing lens in order to minimise the power density at the laser focus. For samples which are subsequently to be used as optical elements, e.g. in eye implant prostheses, it is essential that no local degradation of the material should be caused by the focussed laser beam. The power density used was more than an order of magnitude below that at which such damage might be produced. Scattering geometries of both 90° and 180° were used: the former arrangement has the advantage of having one less reflecting element in the light path, but the latter arrangement is generally more convenient for the mounting of small samples. No significant difference was observed between the Raman line intensity ratios as measured with the two geometries. The spectral slit width was 5cm⁻¹. The photomultiplier was a cooled R.C.A. C31034 tube, this having the advantage of a spectral sensitivity which is not greatly dependent on wavelength. Fluorescence is sometimes a problem in Raman observations on polymeric materials, but no serious problems were encountered with the methyl methacrylate samples. Initial fluorescence could be reduced to a low level by the conventional 'drench-quench' technique, whereby the sample is allowed to remain in the laser beam for a few minutes before the measurement is taken.

Figure 5 shows the experimental relation between the Raman intensity ratio I_{cc}/I_{co} (intensities expressed as peak heights) and w/w% monomer as determined by the gas chromatographic method.

The relation is essentially a linear one over the range studied. In general the observed intensity of a Raman line depends on a number of instrument-independent factors, but many of these are eliminated when intensity ratios are taken. There are a number of wavelength-dependent factors, such as the wavelength dependence of the grating efficiency and of the photomultiplier response, and whether or not the spectrometer slits are programmed. However, because the lines measured are very close in absolute wave-length, these effects are small. Theoretically, integrated intensities i.e. band areas, would be preferable to line heights, since it may be shown that intensity ratios based on the former should be substantially independent of the spectrometer band pass, whereas this may not always be true for intensity ratios based on the latter. However, the experimental determination of band areas effectively requires the measurement of band width, and in practice it is often not possible to estimate band width with as great a precision as band height. This is particularly the case with relatively weak bands. Our observations have shown that the Raman intensity ratio, expressed in terms of peak heights, is effectively independent of slit width over at

least the range 3cm^{-1} to 8cm^{-1} .

The method and apparatus of the invention are directly applicable to the improvement or control of the manufacture of optical implants for human use. It is possible, for example, to provide for each implant to be passed automatically after manufacture, to the spectroscopic testing apparatus for rejection or acceptance according to its monomer content.

The method of the invention is useful for pmma articles other than optical elements. For example, it has utility in other medical areas and in dentistry, where control and knowledge of monomer content in pmma articles is important.

WHAT WE CLAIM IS:—

1. A method of non-destructively assaying an article of polymethylmethacrylate for the free monomer content thereof, which comprises irradiating the article with substantially monochromatic light of a wavelength such as to give rise to, in the Raman spectrum, a pair of lines, one line arising from the monomer alone and the other from both the monomer and the polymer; determining the said pair of lines in the Raman spectrum of the irradiated article and thereby assaying the monomer content in the article.
2. A method according to claim 1, wherein the article is a lens implant of approximate weight 10 mg.
3. A method according to claim 1 or 2 wherein the monochromatic light is generated by a tuned laser.
4. A method according to claim 1, 2 or 3, wherein the monochromatic light is substantially 647.1 , 514.5 or 488.0 nano-metres.
5. A method according to claim 4, wherein the said lines of the pair are at $1640 \pm 10\text{ cm}^{-1}$ and $1730 \pm 10\text{ cm}^{-1}$ in the Raman spectrum.
6. A method according to any of claims 1 to 5, wherein the intensities of the two lines in the Raman spectrum are measured automatically and the monomer content automatically calculated therefrom.
7. A method according to claim 1, substantially as herein described with reference to Figure 1, or Figures 1 and 3, or Figure 4 of the accompanying drawings.
8. A method according to claim 1, substantially as herein described with reference to Figure 2 or Figure 5 of the accompanying drawings.
9. Apparatus for non-destructively assaying an article of polymethylmethacrylate for the free monomer content thereof, which comprises a laser, means for mounting the article in the light path from the laser, a Raman spectrograph for observing the Raman spectrogram of the irradiated article; and means for automatically comparing the intensities of two pre-selected lines in the spectrogram and determining therefrom the monomer content of the article.
10. Apparatus according to claim 9, which also includes means responsive to the determined monomer content to move the article from its mounted position to one of two receiving stations.
11. Apparatus according to claim 9 substantially as herein described with reference to Figure 1 or Figures 1 and 3 of the accompanying drawings.
12. Apparatus according to claim 9 substantially as herein described with reference to Figure 2 of the accompanying drawings.

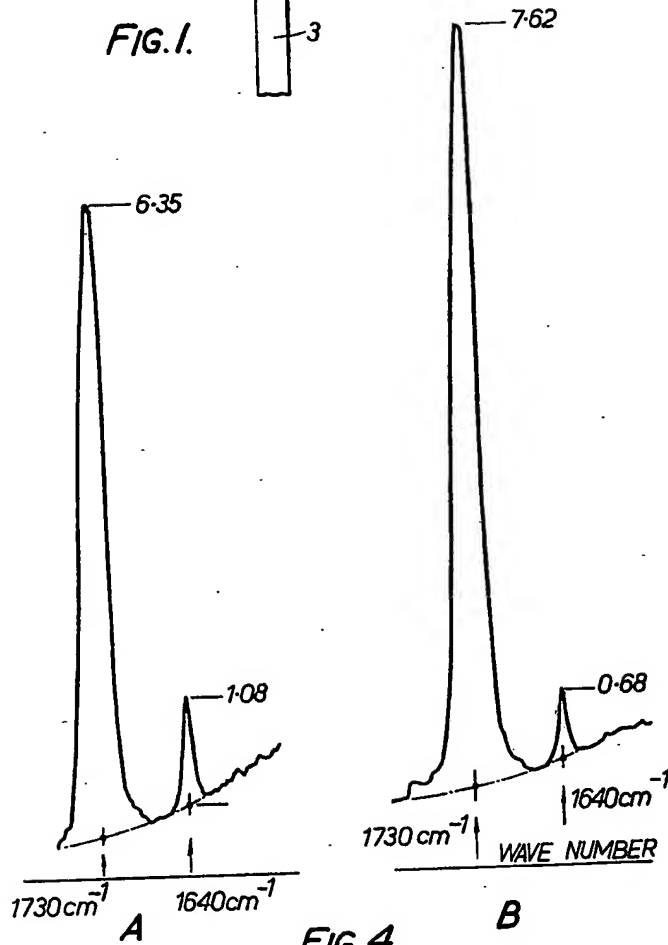
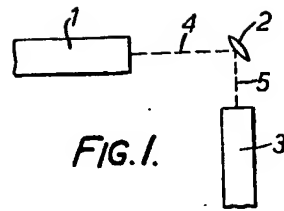
A.A. THORNTON & CO.,
Chartered Patent Agents,
Northumberland House,
303/306, High Holborn,
London, WC1V 7LE.

1528418

COMPLETE SPECIFICATION

4 SHEETS

This drawing is a reproduction of
the Original on a reduced scale
Sheet 1



BEST AVAILABLE COPY

BEST AVAILABLE COPY

1528418 COMPLETE SPECIFICATION

4 SHEETS

This drawing is a reproduction of
the Original on a reduced scale
Sheet 2

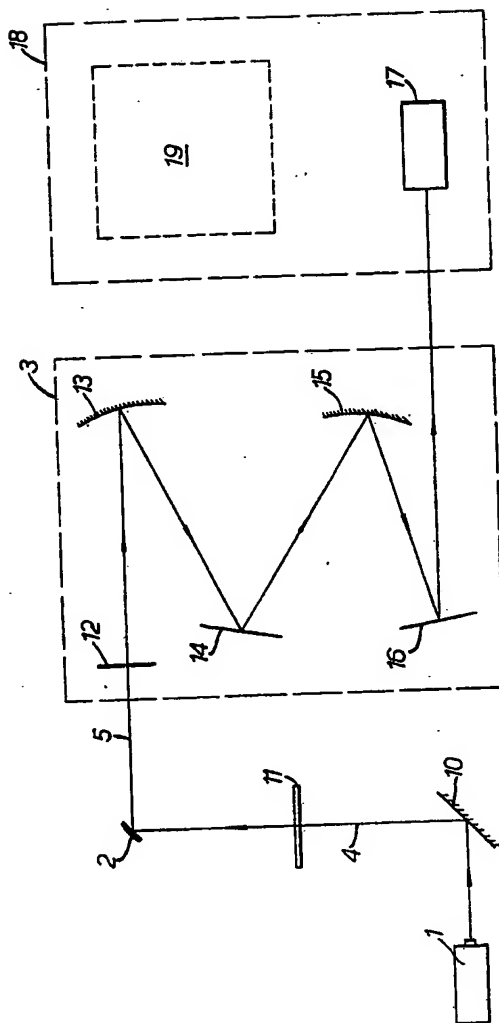


FIG. 2.

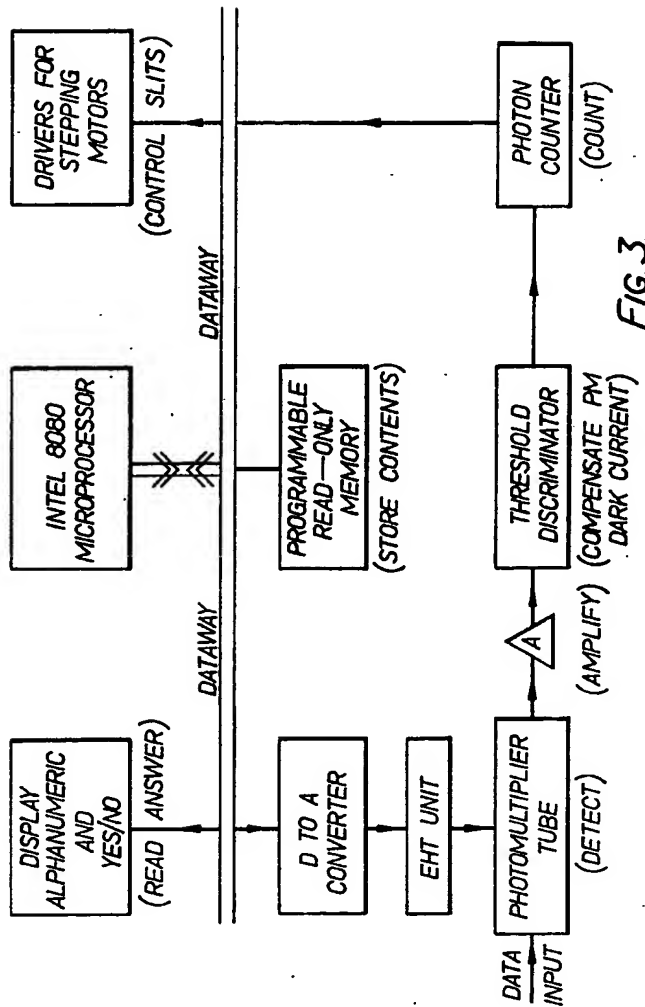


FIG. 3.

BEST AVAILABLE COPY

BEST AVAILABLE COPY

1528418 COMPLETE SPECIFICATION
4 SHEETS This drawing is a reproduction of
the Original on a reduced scale
Sheet 4

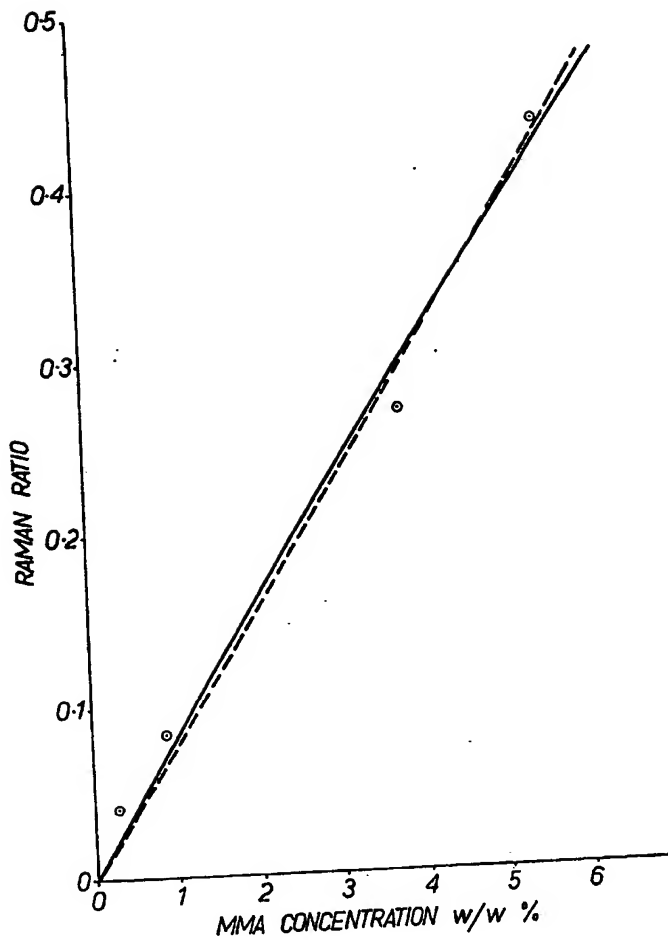


FIG.5.